Tolvaptan for SIADH in Myelodysplastic Syndrome with Blast Crisis

Padmavathi Mali, MD; Sudheer R. Muduganti, MD; Rahaman Mujibur, MD; Narayana Murali, MD

ABSTRACT
Syndrome of inappropriate antidiuretic hormone secretion (SIADH) is a common cause of hyponatremia in cancer patients. It is most frequently reported in association with small-cell lung cancer, but has been reported in other cancers as well. Here we report the case of a patient with myelodysplastic syndrome and blast crisis who developed concurrent hyponatremia. The patient failed to respond to fluid restriction and administration of hypertonic saline. She was treated with tolvaptan, a vasopressin antagonist licensed for the treatment of adult patients with hyponatremia secondary to syndrome of inappropriate antidiuretic hormone secretion. We conclude that in myelodysplastic syndrome patients with blast crisis, inappropriate antidiuretic hormone secretion should be considered as a cause of hyponatremia and be treated with tolvaptan.

CASE PRESENTATION
A 66-year-old woman was admitted to the hospital with chest pain. She had a diagnosis of myelodysplastic syndrome (MDS) and her most recent bone marrow aspirate showed hypercellular marrow with severe reticulin fibrosis and an increase in myeloblasts, suggestive of evolving MDS classified as refractory anemia with excess blasts-2 (RAEB-2). She received 4 cycles of azacitidine as an outpatient in anticipation of getting bone marrow aspiration before the fifth cycle. One week before hospital admission, her sodium level was 135-137 mmol/L (normal 133-144 mmol/L).

The patient was admitted for chest pain described as substernal, pressure-like, and nonpositional. Her physical examination was unremarkable, and her laboratory results showed a white blood cell count (WBC) of 13,700/μL (normal 4,100–10,900/μL) with 6% blast cells, 46% neutrophils, 26% lymphocytes, 11% monocytes, 1% basophils, and 10% myelocytes and metamyelocytes. Additional laboratory results showed normal hemoglobin (11.6 g/dL), platelets (213,000/ml), and creatinine (0.5 mg/dL) with low levels of sodium (133 mmol/L, normal 133-144 mmol/L) and urea nitrogen (5 mg/dL, normal 6–24 mg/dL), and an elevated D-dimer of 2.5 μg/mL (normal 0.1–0.67 μg/mL). A subsequent computed tomography (CT) scan of the chest was negative for pulmonary embolism, but the patient's bones were diffusely sclerotic due to underlying MDS, and this was determined to be the cause of her chest pain. She was started on anticoagulants for pain and continued on her home medications, including fluoxetine.

The next day, the patient's sodium level had dropped to 127 mmol/L, reaching 120 mmol/L in the next 2 days. Although the patient was euvoletic on clinical examination, her laboratory results showed low serum osmolality at 253 mOsm/kg (normal 282-305 mOsm/kg), urine sodium at 45 mmol/L, serum uric acid at 1.8 mg/dL (normal 2.3-6.4 mg/dL), and urine osmolal-
the lung and is rarely seen with other lung tumors.

Hyponatremia from SIADH is a common electrolyte abnormality seen in patients most often due to a small cell carcinoma of the lung and is rarely seen with other lung tumors. Less common causes of malignancy-associated SIADH include head and neck cancers, olfactory neuroblastoma (esthesioneuroblastoma), and extrapulmonary small cell carcinomas. In the literature, there is one other case report of SIADH in a patient with AML with multilineage dysplasia who developed hyponatremia and showed symptoms of SIADH through a mechanism similar to tumor lysis. This is the first case of hyponatremia from SIADH in a patient with myelodysplasia with blast transformation.

Evidence suggests that hyponatremia in cancer patients may be a negative prognostic factor, making recognition and appropriate treatment particularly important. In the patient described here, the diagnosis of SIADH was based on clinical status and laboratory values after ruling out thyroid and adrenal insufficiency. It is also important to exclude the potential influence of drugs on hyponatremia. In the patient presented here, we began treatment of hyponatremia by discontinuing fluoxetine with fluid restriction. Fluoxetine has relatively slow elimination with a half-life of 1 to 3 days after acute administration and 4 to 6 days after chronic administration. The patient had been on fluoxetine for several months before admission with no history of hyponatremia. Sudden development of hyponatremia concurrent with development of AML prompted us to look for other causes, including blast-induced hyponatremia.

In patients with cancer, hyponatremia is often the result of SIADH and is thought to be caused by the ectopic production of arginine vasopressin (AVP) by tumor tissues or the effects of anticancer and palliative medications on AVP production or action. In a single case report in the literature, blast cells were reported to stain positive for ADH in a patient with AML and SIADH. In the present case, bone marrow was negative for ADH by immunohistochemical staining, but the interpretation and pathology results may be of limited value due to decalcification of the sample. Therefore, we are unable to rule out the tumor tissue as a source of ADH.

In the treatment of hyponatremia, hypertonic saline is in-

<table>
<thead>
<tr>
<th>Day</th>
<th>Serum Sodium (mmol/L)</th>
<th>Intervention</th>
<th>Urine Osmolality (mOsm/kg)</th>
<th>Urine Sodium (mmol/L)</th>
</tr>
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<tbody>
<tr>
<td>-7</td>
<td>137</td>
<td>Admission</td>
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<tr>
<td>0</td>
<td>133</td>
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<td>566</td>
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<tr>
<td>4</td>
<td>120</td>
<td></td>
<td>253</td>
<td></td>
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<tr>
<td>5</td>
<td>117</td>
<td>Intensive Care Unit and 3% saline</td>
<td>691</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>122</td>
<td>Fluoxetine discontinued, fluid restriction</td>
<td>425</td>
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</tr>
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<td>7</td>
<td>122</td>
<td>Fluid restriction</td>
<td>691</td>
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<tr>
<td>8</td>
<td>122</td>
<td>Fluid restriction, tolvaptan (15 mg)</td>
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<tr>
<td>10</td>
<td>129</td>
<td>Fluid restriction, tolvaptan (15 mg)</td>
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<tr>
<td>11</td>
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Retrospectively, the bone marrow biopsy was sent for immuno-

## DISCUSSION

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REFERENCES


CONCLUSION

The etiology of hyponatremia is diverse, and systemic evaluation is important for defining the cause and formulating a treatment plan. SIADH should be considered as a potential cause of hyponatremia in MDS patients with blast crisis. The vasopressin antagonist tolvaptan can be used to correct the hyponatremia if conservative treatments fail.
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